Hemodynamic Effects of Sleep Restriction and Laboratory Stress

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Abstract

The reactivity hypothesis of hypertension states that persistent and exaggerated blood pressure (BP) responses to common stressful events may lead to the development of hypertension and cardiovascular disease. This experiment aimed to examine hemodynamic profile induced by behavioural challenges in the form of sleep restriction and psychosocial stress induced by time-pressured cognitive performance. Participants were 96 healthy male and female adults who received 40% of their usual overnight sleep on 2 of 4 nights preceding 4 morning visits to the research laboratory. Consistent with previous studies, sleep restriction had no appreciable effect on BP level. However, Finapres measurements of CO and TPR showed that the null effect of sleep restriction on BP concealed a pronounced vascular response in the form of marked increases in TPR, suggesting that a lifestyle characterised by persistent sleep loss could contribute significantly to the development of cardiovascular disease.

Hemodynamic Reactivity

Persistent blood pressure responses to frequently encountered pressor agents (e.g., stressful events) may be a risk factor for later development of hypertension and coronary heart disease (Fredrikson & Matthews, 1990; Manuck, Kasprowicz, & Muldoon, 1990). This proposition, known as the reactivity hypothesis, has spawned extensive experimentation of hemodynamic responses to laboratory analogues of stressful events (e.g., performance of psychomotor and cognitive tasks).

The reactivity hypothesis presupposes a degree of laboratory-to-life generality, and this assumption is supported by a substantial body of epidemiological evidence including prospective and case-control studies (e.g., Jennings et al., 2004; Treiber et al., 2003). Nevertheless, the amount of variance in "real world" morbidity explained by reactivity to standard laboratory assessment has generally been modest, prompting closer scrutiny of underlying mechanisms in the expectation that such knowledge will yield findings having important clinical implications (e.g., Kamarck & Lovallo, 2003). The present study is part of this new thrust, and extends previous work by us on *hemodynamic profile* as a key mechanism of blood pressure reactivity (Colverson, James, & Gregg, 1996; Gregg, James, Matyas & Thorsteinsson, 1999; Gregg, Matyas & James, 2002; Gregg, Matyas & James, 2005; James & Gregg, 2004a; Ottaviani, Shapiro, Goldstein, James, & Weiss, 2005; Thorsteinsson, James, Gregg, 1998).

Viewing sleep loss as a potential source of psychophysiological stress, prospective and case-control epidemiological studies show that sleep complaints and short sleep duration are associated with increased cardiovascular morbidity and mortality (e.g., Ayas et al., 2003; Kripke et al., 2002; Meier-Ewert et al., 2004). Nevertheless, direct evidence of the effects of sleep loss on hemodynamic variables remains inconsistent and puzzling. In particular, studies have repeatedly found little or no acute effect of sleep restriction on blood pressure and heart rate (e.g., Kato et al., 2000; Meney et al., 1998).

Aim

The main aim of the present study was to characterise the hemodynamic effects induced by sleep restriction and laboratory stress. While no specific prediction was made regarding the effect of sleep restriction on blood pressure (due to conflicting evidence), hemodynamic profile (explained below) was examined as a possible means for clarifying inconsistencies in previous findings.

Hemodynamic Profile

It is well-established that blood pressure responses of similar magnitude may be accompanied by different patterns of change in cardiac output (CO) and total peripheral resistance (TPR). In particular, stable patterns of CO and TPR have been observed over time for the same people and for similar tasks performed by different people, leading to the conclusion that in-

dividual differences in hemodynamic response patterns may be implicated in cardiovascular pathology (e.g., Gregg et al., 1999, 2002).

Hemodynamic profile describes the system of homeostatic regulation of blood pressure whereby an increase in either CO or TPR tends to be accompanied by a decrease in the other variable (e.g., Guyton, 1987; Gregg et al., 2002). Individual differences in hemodynamic response patterns following psychological challenges are predictive of susceptibility to hypertension (e.g., Kamarck & Lovallo, 2003; Matthews et al., 2002). Indeed, given that blood pressure responses of similar magnitude may be accompanied by markedly different patterns of CO and TPR reactivity, there is considerable interest in the possibility that hemodynamic profile might predict cardiovascular risk more reliably than blood pressure reactivity alone.

The terms *myocardial and vascular reactivity* have been used to describe hemodynamic responses characterised, respectively, by increases in CO (predominance of alpha-adrenergic responding) and by TPR (predominance of beta-adrenergic responding) (e.g., Lawler et al., 1995). To date, most studies of individual differences in hemodynamic profile have attempted merely to assign individuals to categories such as myocardial responder or vascular responder. Our group has shown that such attempts are fundamentally flawed (Gregg et al., 2002). To begin with, there is no consensus as to the most suitable method of classification. Moreover, the likelihood of consensus is remote, given that categorical approaches force discontinuity onto what are in fact continuous distributions of measurements. Furthermore, none of the attempted classification methods gives sufficient attention to the reciprocal relationship between CO and TPR well known in cardiovascular physiology. In response to these shortcomings, we developed a model, expressly derived from physiological theory, which explains variations in blood pressure in terms of hemodynamic profile characterised as a dynamic compensatory relationship between CO and TPR (Gregg, Matyas & James, 2002; James & Gregg, 2004a; Ottaviani, Shapiro, Goldstein, James, & Weiss, 2005).

One problem with previous approaches is that they confound two separate concepts, **compensation deficit** and hemodynamic **profile**, which can be independently expressed. Compensation deficit measures the **extent** to which CO and TPR compensate, thereby indicating degree of change in blood pressure level (increase, decrease, or no change). On the other hand, hemodynamic profile measures the **nature** of the compensation, whether it is myocardial (CO predominates) or vascular (TPR predominates) or both (i.e., a "mixed response" involving equal amounts of change in CO and TPR). The validity of the model as demonstrated by its originators (Gregg et al., 2002) has been subsequently confirmed (James & Gregg, 2004a; Ottaviani et al., 2005). Part of the importance of this work is that hemodynamic profile appears to be implicated in the development of cardiovascular pathology. Specifically, it is believed that blood pressure changes characterised as vascular confer increased risk of disease (e.g., Julius, 1988).

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Method

Participants

A total of 96 healthy volunteers, consisting of 54 females and 42 males, were recruited from amongst the university student community. All were normotensive (blood pressure less than 140/90 mmHg), were not taking any prescription medication, and were not consulting a physician for any medical condition at the time of the study. Participants ranged in age from 17-52 years (mean of 19 years), with body mass index (kg/m2) of 18-28 for females and 18-29 for males.

Design

Participants maintained a sleep diary for six consecutive days, yielding information on lights-out time, time to fall asleep (sleep latency), times and duration of nighttime awakenings (sleep fragmentation) and time of final awakening. They attended 4 laboratory sessions on the same day of the week for 4 consecutive weeks. On 2 of 4 nights preceding their visits to

the research laboratory, participants experienced 40% of their usual overnight sleep. For example, a participant who typically retired at 23.30 and awoke at 07.00 with no sleep fragmentation (7.5 hours of sleep) would be awakened at 02.30 after having had 3 hours sleep. Participants had no further sleep before undertaking the laboratory visit scheduled for that same day.

To encourage adherence to the sleep regimen, participants were provided with an "activity pack" consisting of printed instructions, activities (e.g., crosswords, puzzles, moderate exercises) and a snack. To monitor actual adherence, participants were provided with a wrist activity monitor (Actiwatch-Alert, Cambridge Neurotechnology Ltd, Cambridge, UK), as this type of measurement has been found to provide valid records of sleep activity (Coffield & Tryon, 2004; Wolfson, Carskadon, Acebo et al., 2003).

Hemodynamic Measurement

Beat-to-beat blood pressure and heart rate were measured non-invasively using a Finapres 2300e Continuous NIBP Monitor, Model (Ohmeda, Madison, WI, USA). In addition to recording systolic and diastolic blood pressure and heart rate, Finapres measurements were analysed using the pulse contour method performed by the "Modelflow" program developed specifically for deriving estimates of cardiac output (CO) and total peripheral resistance (TPR) (Wessling, Jansen, Settels, & Schreuder, 1993). The methodology has been reported to compare favourably with a variety of alternatives (e.g., Stok, Baisch, Hillebricht, Schulz, Meyer, & Karemaker 1993), including intra-arterial recording (Voogel & van Montfans, 1997).

Laboratory Stress

The participant was seated in one room of a sound-attenuated, temperature-controlled suite. After the blood pressure monitor was attached, the experimenter left the room and supervised the experiment from an adjoining room via audiovisual linkage. The experiment proper began with a 5-minute baseline phase. This was preceded by a 10-minute rest period incorporating the principle of the "vanilla baseline" (Jennings, Kamarck, Stewart, Eddy & Johnson, 1992), which involves participants reading "neutral" magazines (e.g., travel, nature). The laboratory stressor consisted of performance-based activities typical of previous reactivity research.

Results

Main effects (expressed as difference scores) for SBP and DPB of the stressor task and sleep restriction are shown in Figure 1. Consistent with previous findings, the laboratory stressor was significantly reactive for both SBP and DBP. Conversely, there was no acute reactive effect of sleep restriction on either SBP or DBP.

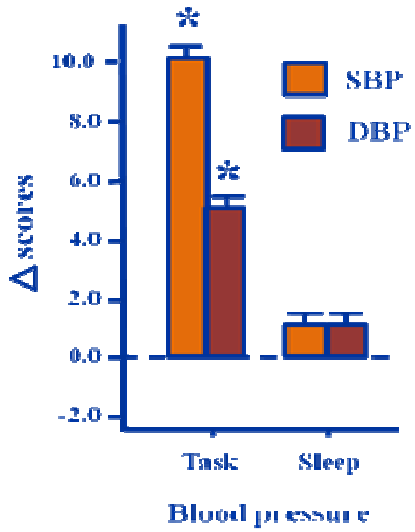

Figure 1. Main effects (expressed as difference scores) for systolic (SBP) and diastolic blood pressure (DPB) during a laboratory stressor (Task) and after sleep restriction (Sleep). *p < .001.

Figure 2, however, shows a very different pattern for hemodynamic profile. The units of measurement are reactivity scores expressed as log ratios. The dotted line represents a reactivity level of zero (i.e., no change from resting baseline). The stressor task produced a significant result for compensation deficit in the positive direction (i.e., reciprocal changes in CO and TPR did not fully compensate), consistent with BP increases evident in Figure 1. On the other hand, scores for compensation deficit did not deviate significantly from zero for sleep restriction. Figure 2 also shows that the hemodynamic profile of the BP increases induced by the laboratory task may be characterised as "mixed" (i.e., neither CO nor TPR increases predominate). In contrast, sleep restriction had an effect on hemodynamic profile indicative of

a marked vascular response (highly significant positive score).

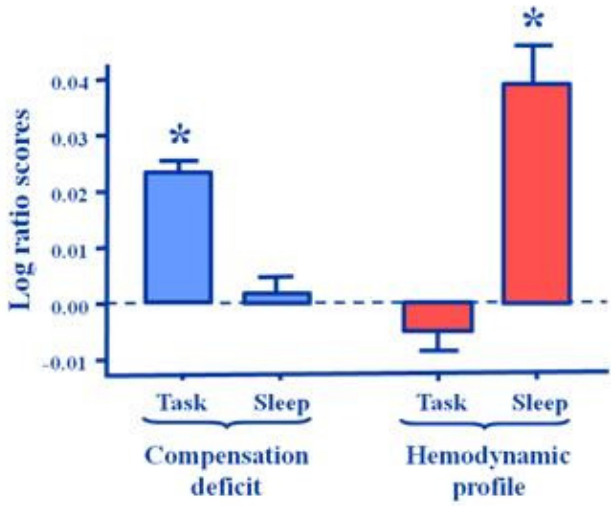

Figure 2. Main effects (expressed as log ratio scores) for compensation deficit and hemodynamic profile during a laboratory stressor (Task) and after sleep restriction (Sleep). *$p <$ .001

Summary and Conclusions

Sleep restriction had no effect on BP level during either a resting or a time-pressured performance task. Conversely, sleep restriction had a marked effect on HP, inducing a vascular profile.

That is, on one hand, epidemiological studies indicate that chronic sleep loss contributes to the development of hypertension and cardiovascular disease. On the other hand, experimental studies indicate that sleep loss has little or no acute effect on blood pressure level. These finding suggest that it may be induced vascular profile (despite no acute effect on BP level) that over time represents a risk to cardiovascular health.

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